

REFERENCES

1. Charlton M, Everson GT, Flamm SL, et al. Ledipasvir and sofosbuvir plus ribavirin for treatment of HCV infection in patients with advanced liver disease. *Gastroenterology*. 2015;149:649-659.
2. Manns M, Samuel D, Gane EJ, et al. Ledipasvir and sofosbuvir plus ribavirin in patients with genotype 1 or 4 hepatitis C virus infection and advanced liver disease: a multicentre, open-label, randomised, phase 2 trial. *Lancet Infect Dis*. 2016;16:685-697.
3. Mecci AJ, Kemos P, Leen C, et al. The association between hepatocellular carcinoma and direct-acting anti-viral treatment in patients with decompensated cirrhosis. *Aliment Pharmacol Ther*. 2019;50:204-214.
4. Toyoda H, Kumada T, Tada T, et al. The impact of HCV eradication by direct-acting antivirals on the transition of precancerous hepatic nodules to HCC: a prospective observational study. *Liver Int*. 2019;39:448-454.
5. Foster GR, Irving WL, Cheung MC, et al. Impact of direct acting antiviral therapy in patients with chronic hepatitis C and decompensated cirrhosis. *J Hepatol*. 2016;64:1224-1231.
6. Nahon P, Layese R, Bourcier V, et al. ANRS CO12 CirVir Group. Incidence of hepatocellular carcinoma after direct antiviral therapy for HCV in patients with cirrhosis included in surveillance programs. *Gastroenterology*. 2018;155:1436-1450 e6.
7. Carrat F, Fontaine H, Dorival C, et al. ANRS CO22 Hepather cohort. Clinical outcomes in patients with chronic hepatitis C after direct-acting antiviral treatment: a prospective cohort study. *Lancet*. 2019;393:1453-1464.
8. Holmes JA, Rutledge SM, Chung RT. Direct-acting antiviral treatment for hepatitis C. *Lancet*. 2019;393:1392-1394.

DOI: 10.1111/apt.15363

Editorial: the increasing burden of microscopic colitis

Microscopic colitis (MC) is a worldwide emergent cause of watery chronic diarrhoea in adults.^{1,2} Initially considered a rare disease, several epidemiological studies reported an increasing incidence over time with similar incidence rate of Crohn's disease or ulcerative colitis, especially in women and elderly patients.^{3,4} However, both regional^{3,4} and nationwide⁵⁻⁷ studies have often shown heterogeneous results in terms of incidence rate, trends and distribution among collagenous colitis (CC) and lymphocytic colitis (LC), the two main subtypes of MC (Table 1).

In a recent issue, Bergman et al explore the incidence rate of MC in Sweden over a 20-year period using a national pathology registry with combination of clinical data.⁸ Notably, this registry was previously validated performing a retrospective review of the medical charts of 215 randomly selected MC pathology records from 15 pathology departments.⁹ Although this validation process involved a small subset of MC incident cases (0.07%) from five counties, the resulting 95% positive predictive value represents a unique and solid basis to minimise the risk of false positive diagnosis and reliably estimate the real incidence of MC in Sweden.⁹

Consistent with two recent nationwide cohort studies from Denmark⁶ and the Netherlands,⁷ the study from Bergman et al confirms the MC incidence rise also in Sweden (up to 10.7 cases/100 000 person-years).⁸ The Swedish study, however, has a longer follow-up (20 years, 1995-2015) revealing a stabilising trend in recent years.⁸ Interestingly, two consecutive population-based studies from the Olmsted County in 1985-2001 and 2002-2010¹⁰ described the same plateau effect. The spread of MC-related risk factors, together with an ameliorated access to colonoscopy, number of colonic biopsies and clinical awareness are regarded as the main drivers of this figure.

A predominance for the LC subtype was found in Bergman et al study, in accordance with pooled incidence rate reported in a

previous meta-analysis.³ On the contrary, the three previous nationwide studies from Iceland,⁵ Denmark⁶ and the Netherlands⁷ as well as other regional or local studies in Sweden^{3,10} contradict this. Resolving this apparent discrepancy remains an unresolved research question. There is a risk of misclassification between the two main subtypes due to: patchy distribution of the thickened collagen band compared with the more general increase in the intraepithelial lymphocyte count⁸; variation in pathologists' practice and histological stains applied, especially in borderline cases¹; no homogeneous pre-defined diagnostic protocol (number of biopsies or other explorations to rule out other diagnosis); and other genetic or environmental influencing factors.

Well-designed epidemiological and case-control studies are still necessary to determine the precise burden of MC and of its two main subtypes (CC and LC) worldwide. Nonetheless, the clinical perception of MC is remarkably changed 40 years after their discovery. In 2019, the sum of evidence requires us to think about MC, consider it during colonoscopy and always take biopsies throughout the colon.

ACKNOWLEDGEMENT

Declaration of personal interests: None.

LINKED CONTENT

This article is linked to Fernandez-Bañares et al paper. To view this article, visit <https://doi.org/10.1111/apt.13477>.


Danila Guagnozzi¹
Gian Eugenio Tontini²
Luca Pastorelli³ 

TABLE 1 Epidemiological studies on microscopic colitis

First author (year)	Country/city	MC incidence (95% CI)	CC incidence (95% CI)	LC incidence (95% CI)
Nationwide studies				
Agnarsdottir (2002)	Iceland	NA	5.2 (4.1–6.6)	4 (3–5.2)
Agnarsdottir (2002)	Denmark	4.6–24.7 ^a	2.9–14.9 (NA) ^a	1.7–9.8 (NA) ^a
Agnarsdottir (2002)	The Netherlands	3.4 (3.3–3.5)	1.8 (1.7–1.8)	1.3 (1.2–1.3)
Agnarsdottir (2002)	Sweden	7.2 (5.6–8.7)	NA	NA
Swedish studies				
Bohr (1995)	Örebro	NA	1.8 (1.2–2.4)	NA
Olesen (2004)	Örebro	NA	4.9 (3.6–6.2)	4.4 (3.1–5.7)
Vigren (2012)	Skane	NA	5.4 (4.3–6.5)	NA
Thorn (2013)	Uppsala	NA	7 (NA)	4.8 (NA)
Wickbom (2013)	Örebro	10.2 (8.7–11.7)	5.2 (4.2–6.3)	5 (4–6)
Davidson (2018)	Skane	NA	5.9 (4.6–7.3)	2.7 (1–4.3)

Abbreviation: NA, not available.

^aIncidence rate of MC, CC and LC in 2002 and 2011 years.

¹Department of Gastroenterology, Hospital Universitari Vall d'Hebron, Translational Mucosal Immunology, Digestive System Research Unit, Vall d'Hebron Institut de Recerca, Centro de investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Barcelona, Spain

²Gastroenterology and Endoscopy Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Department of Pathophysiology and Organ Transplantation, University of Milan, Milan, Italy

³Gastroenterology Unit, IRCCS Policlinico San Donato, San Donato Milanese, Italy
Email: luca.pastorelli@grupposandonato.it

ORCID

Luca Pastorelli  <https://orcid.org/0000-0002-2810-9951>

REFERENCES

- Miehlke S, Verhaegh B, Tontini GE, Madisch A, Langner C, Münch A. Microscopic colitis: pathophysiology and clinical management. *Lancet Gastroenterol Hepatol*. 2019;4:305–314.
- Fernández-Bañares F, Casanova MJ, Arguedas Y, et al. Current concepts on microscopic colitis: evidence-based statements and recommendations of the Spanish Microscopic Colitis Group. *Aliment Pharmacol Ther*. 2016;43:400–426.
- Tong J, Zheng Q, Zhang C, Lo R, Shen J, Ran Z. Incidence, prevalence and temporal trends of microscopic colitis: a systematic review and meta-analysis. *Am J Gastroenterol*. 2015;110:265–276.
- Fumery M, Kohut M, Gower-Rousseau C, et al. Incidence, clinical presentation and associated factors of microscopic colitis in Northern France: a population-based study. *Dig Dis Sci*. 2017;62:1571–1579.
- Agnarsdottir M, Gunnlaugsson O, Orvar KB, et al. Collagenous and lymphocytic colitis in Iceland. *Dig Dis Sci*. 2002;47:1122–1128.
- Bonderup OK, Wigh T, Nielsen G, Pedersen L, Fenger-Gron M. The epidemiology of microscopic colitis: a 10-years pathology-based nationwide Danish cohort study. *Scandinavian J Gastroenterol*. 2015;50:393–398.
- Verhaegh B, Jonkers DM, Driessen A, et al. Incidence of microscopic colitis in the Netherlands. A nationwide population-based study from 2000 to 2012. *Dig Liv Dis*. 2000;2015:30–36.
- Bergman D, Clements MS, Khalili H, Agréus L, Hultcrantz R, Ludvigsson JF. A nationwide cohort study of the incidence of microscopic colitis in Sweden. *Aliment Pharmacol Ther*. 2019;49:1–6.
- Svensson M, Bergman D, Olén O, et al. Validating microscopic colitis (MC) in Swedish pathology registers. *Scandinavian J Gastroenterol*. 2018;53:1469–1475.
- Davidson S, Sjöberg K, Engel P, et al. Microscopic colitis in Denmark and Sweden: incidence, putative risk factors, histological assessment and endoscopic activity. *Scand J Gastroenterol*. 2018;53:818–824.